

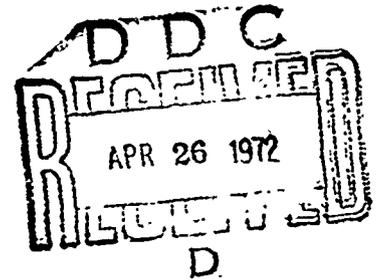
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AEROSPACE STRESS AND HUMAN RELIABILITY

AFOSR 69 - 1821

Terminal Report, 1972



Amedeo S. Morrazzi, M.D.
Principal Investigator

University of Missouri Institute of Psychiatry
St. Louis, Missouri

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13. ABSTRACT Interaction with the external and internal environments is dependent on the information retrieval process. The interneuronal communication process essential to information retrieval and to cerebral integration generally has been the object of extensive study utilizing evoked field, focal, and extra- and intra-cellular unitary potentials as measures of synaptic output. In the process the investigators have worked out a means of checking adequacy of retrieval from association areas, which has enabled them to convert experimental findings into clinical test procedures able to assess "breakdown point" in subjects without actually breaking them down. This could be modified so as to behaviorally detect drug abusers and, with modification, detect drug abuse and its lasting consequences.			

Abstract

Coping behavior and specific performance depends on adequate use of past experience, including special training to generate appropriate responses. These may be close copies of previous performances or modifications suitable to the relation of the new situation to the model generalized from the sum of related past experiences.

The stored information required to supply the solutions to the problems - large and small - presented by the almost continuous stream of situations, in daily living and dramatically intensified in combat, must first of all be retrieved and mobilized.

Thus interaction with reality, i.e., the external and internal environments is certainly dependent on the information retrieval process. This has therefore become a focus of the studies supported by the Air Force Office of Scientific Research Project on "Aerospace Stress and Human Reliability". It has involved normal individuals, behaviorally disturbed patients manifesting difficulty in "reality checking" and laboratory animals in which cerebral function could be monitored while experimentally manipulated or disturbed.

The interneuronal communication process essential to information retrieval and to cerebral integration generally has been the object of extensive study utilizing evoked field, focal, and extra- and intra-cellular unitary potentials as measures of synaptic output. In the process we have worked out a means of checking adequacy of retrieval from association areas, which has enabled us to convert our experimental findings into clinical test procedures able to assess "breakdown point" in subjects without breaking them down. This could also be modified so as to behaviorally detect drug abusers and, with modification, detect drug abuse and its lasting consequences.

Introduction

A rationale for the clinical assessment procedures has evolved from a theory of inadequate coping behavior or failure of homeostasis - with psychosis as a cardinal manifestation - which grew out of the studies of cerebral synaptic transmission in health and disease.

Correspondence of electrical signals recorded simultaneously from populations and individual constituent cells showed that they could indeed be utilized to monitor and meaningfully analyze cerebral activity at the respective levels.

Cerebral Homeostasis

Such monitoring revealed an equilibrium state between excitation and inhibition at all cerebral synapses, sampled at cortical, subcortical, brain stem and cerebellar levels. A physiological transaction in this system consists of a transient biasing of equilibrium, by an increment in input, in favor of a preponderance of inhibition or excitation such that the cause of the input will be removed and normally a rapid restoration of equilibrium taking place. The consequences of this local homeostasis are amplified and varied by the multitude of additional circuits with which it is linked and forms an integral part.

Direct and indirect evidence from these studies both show that transmission across the synaptic gap is effected by excitatory and inhibitory chemicals or neurohumors, whose action is consistent at all synapses but whose ultimate effect depends on the complexities of the circuits controlled. At the circuit level, homeostasis begins with negative feed-back. When this is in its turn inhibited the released synapses show increased activity, i.e., a secondary excitation. When excitatory neurohumors are caused to accumulate another secondary effect, paralysis, may follow the primary excitation.

Experimental Alteration of Synaptic Neurohumoral Environment

When manipulating the synaptic chemical, i.e., neurohumoral environment either by modifying the quantities of neurohumor present or by the addition of drugs, it needed to be demonstrated that the potential attendant circulatory changes that might be caused do not

complicate the observations. This was accomplished by use of an oxygen electrode adjacent to the potential recording electrode on the surface of the cortex. The oxygen electrode showed that at the low doses, used so that major effects would be limited to the brain, there is no accompanying reduction in oxygen availability to the brain cells generating the recorded signals.

By intracellular recording we have been able to demonstrate the classical characteristics of membrane changes for the actions studied, i.e., EPSPs and IPSPs respectively with associated changes in transmembrane resistance.

The varied individual nature of the members we have studied of the excitatory substances, acetylcholine and glutamate and the inhibitory ones, norepinephrine, epinephrine, dopamine, serotonin, GABA and Glycine, suggest possible specificity in different aspects of the information handling they control with possible access to these by suitable drugs, whose use in human testing will be described in a later part of this report.

Such chemicals and drugs are drawn from the analogs, homologs or modifiers of the neurohumors. These compounds may be completely foreign to the body, or toxins originated by the body, in some cases as products of perverted metabolism of the neurohumors. This project has studied hallucinogens, of the catechol and indole amine series and tranquilizers in the former group and DMPEA, along with related biogenic amines and a taraxein-like small moiety, adsorbed to blood proteins found in high titer in the serum of certain schizophrenics, in the latter.

The work has shown that all of the above distort synaptic equilibrium towards excess inhibition and, further, that tranquilizers can preempt the inhibitory receptors and thereby, by substituting their weak inhibitory action, protect against the stronger biogenic amine inhibitors. This is the basis of tranquilizer action by phenothiazines, rauwolfia alkaloids, propane diols and diazepam and also accounts for the nature of their central nervous system toxic actions which naturally, therefore, resemble those of the hallucinogens and

psychotomimetics they were intended to offset.

The specificity of the various synaptic inhibitors and of the respective receptors has been clarified by finding differential blocking agents. In brief, chlorpromazine (CPZ) blocks only the catechol and indole amines, triptelenamine only histamine, bicuculline only gamma-aminobutyric acid (GABA) and glycine, while strychnine blocks all. Atropine blocks acetylcholine but not glutamate. On the other hand, dilantin enhances and prolongs only GABA.

Pharmacological Synaptic Characterization and A Basic Generalization

The use of the various chemical and drug manipulations to pharmacologically characterize cerebral synapses has uncovered the important basic generalization that all cerebral synapses are qualitatively alike with only quantitative differences in their receptors and, therefore, in their neurohumoral systems. This project has substantiated these findings at the cortical, subcortical, brain stem and cerebellar levels. The difference in thresholds is the clue to the disorganizing effects of attempts to influence neurohumoral transmission and conversely of the possibilities for correction when functional disorganization is already present.

Behavioral Counterparts

Before considering this in detail it will be useful to briefly review the behavioral counterparts and, in fact, consequences of the synaptic phenomena described, subject to the reservation that the actual synapses involved in the particular paradigms were not determined. As a continuation of previous work in rats and cats, a time discrimination version of a food-rewarded lever pressing behavior in monkeys, and cigarette-rewarded behavior in patients on our research ward was carried out. Both showed a sequence of dose-related effects that paralleled the synaptic inhibitory effects of LSD, i.e., disinhibition or release phenomena in the earliest phase (smallest absorption and therefore smallest dose) producing impaired time discrimination manifested as premature responses, slowed performance with increased absorption and return of premature responses as tissue drug concentration wanes. In the patients, the LSD (subclinical doses producing no overt effects) resulted in an intensification of their placebo

response abnormal pattern. Acute CPZ administration terminated the LSD effect, with chronic administration improving temporal discrimination in a manner resembling the acute antagonism of LSD. Adequate doses of chronically administered chlorpromazine similarly were able to improve the abnormal placebo pattern. Larger doses in monkeys aggravated instead of antagonizing the LSD effects, just as with the synaptic actions monitored electrically and in agreement with the toxic psychosis produced by the larger doses in man.

Practical Human Testing

The practical application of these fundamental studies of the normal and drug taxed or challenged nervous system, designed to supply the neuropharmacological and conceptual basis for the study of stress and human reliability, has kept pace and produced testing instruments and procedures, which we have been utilizing in college students and in patients on our research ward.

These studies can be best understood by considering our demonstration, by simultaneous electrical recording from the primary visual receiving and from an association or reference area, that the latter had a lower threshold to the action of synaptic inhibitors, including LSD and amphetamine.

LSD had been of interest all along because it could reversibly produce behavioral patterns characterized by dissociation, e.g., hallucination. Thus, this manifestation of inadequate use of stored information could be accounted for by the fact that LSD limited communication with association or information storage areas. Such inadequate access to stored past experience would make reality checking difficult, and therefore result in hallucination, which then must be regarded as an aberrant perception, i.e., an erroneous judgment or interpretation of the new information arriving at the primary receiving area.

Such difficulty in reality checking and the resulting erroneous judgment and perception would seriously impair human reliability, especially under stress. So this aspect of inadequate cerebral integration became a particularly relevant measure of an important factor in

human reliability. Extension of this concept to patients with a persistent loss of reliability, the mentally disturbed, offered an explanation of hallucination and a view of psychosis as an extensive dissociation or failure of cerebral integration.

Reliability could be tested both in normal college students and in patients by measuring their response to a challenge to proper information retrieval, a factor indispensable to reliability. This was done by introducing a transient impediment to such retrieval by administering LSD or amphetamine, which we showed to have the same effect.

Air Force Needs

Focusing more directly on the Air Force objectives, which are really human engineering requirements, we need to realize: -

1. That, since information retrieval is the initial, basic step in performance it is an essential and probably most important factor to be measured in assessing the reliability of a trained person, who is not expected to have motor incoordination of a primary origin, i.e., other than due to uncertainty resulting from impaired decision making to which, among others, an inadequate proprioceptive information feed-back contributes.
2. Objective, instrumental, simple tests are required that can be carried out by relatively non-skilled personnel in the field, and that are easy to analyze either locally, or centrally. In the latter case analysis could be facilitated by computerization.
3. Identity and nature of testing should not be so obtrusive as to be disturbing to subjects and prevent acceptance as a routine procedure.
4. Testing should be a valid predictor of "break-down point" under stress without actually "breaking down" or impairing normal performance immediately subsequent to or as an aftermath of the testing.
5. Testing should be capable of detecting latent difficulties that may never have

become overt to date, but possibly could be corrected without ever becoming overt.

6. Testing should be capable of detecting undue rigidity in the manner in which subjects relate to environment with loss, therefore, of adequate flexibility to adapt to and solve infrequent or even unforeseen situations.

The tests that have been developed fulfill these criteria. On the basis of the rationale presented above we tested information retrieval as evidenced by its mobilization and use in the solution of a perceptual conflict. This was induced by presenting new information which was at the same time both incongruous and congruous with long established experience and training. To the extent that the stored congruous information becomes less available, the conflict is resolved in favor of undue acceptance of the new, deviant information.

Visual Perceptual Conflict

The perceptual conflict is achieved in the visual modality by presenting disparate images to the two eyes by viewing the interior of a room through an aniseikonic lenses. After binocular fusion (for whose normal capacity the subject is pretested) this results in a distortion of the room taking place in competition with cues (monocular) which remind the subject, on the basis of past experience, that rooms are not usually distorted. Perceived "reality" then depends on the extent to which stored information determines the predominance or weighting of previous training over the newest experience. The developing apparent slope of the boundaries of the distorted room are tracked by a guide bar which the subject maintains, by remote control, parallel to a selected boundary, e.g., the line formed by the junction of the left and the rear walls of the room. Movement of the guide bar provides continuous monitoring which is automatically recorded.

Each test session consists of a (self) control period of measurements of the unmodified perceptual conflict, followed by a period in which access to stored information is reduced by giving a subclinical dose (producing no overt symptoms) of a substance able to dissociate

brain function, thus serving as a challenge to subsequent performance during the duration of drug effect. The dose of LSD in adults or amphetamine in children is calculated to produce no change in the resolution of the problem in normals. When, however, there is already some difficulty - small enough to be considered latent - the addition of the challenge renders the sum of the two manifest. The result is in favor of acceptance instead of censoring out perceptual distortion or the miniature laboratory semblance of an hallucination that has been induced by the aniseikonic lenses.

In patients this, then, measures intensity of illness and in non-patients it measures tendency to an inadequate judgment of conflict situations, and therefore reduced reliability under trial and stress as in military operations, especially in combat.

Auditory Perceptual Conflict

Similarly, we have devised and tested an analogous procedure using (presently more conveniently) the auditory modality. This relies on the necessity for the individual to continuously monitor his emitted sounds and sound combinations to check that they are the words, phrases, etc., required to conduct normal speech. Thus, the speaker continuously listens and immediately corrects and modulates his speech when necessary. When the required auditory feed-back is limited to the output of head phones connected to a play-back head on a tape recording the subject's speech, the play-back can be delayed by moving the play-back head to a later position on the tape. When the lack of synchrony between recorded and feed-back sound is great enough, speech impairment and ultimately stuttering takes place.

This auditory perceptual conflict, which is in time rather than in space as in the case of the visual, produces unreliable speech performance. The degree of reliability can be measured by noting the maximum delay (moving play-back head away from recording head on tape) that can be tolerated and still have normal (actually minimally impaired) speech. This equipment already fits military needs in requiring only a slight modification of light-weight, readily available tape recorders.

Demonstrated Test Capability

In both tasks the final reading is the difference between pre- and post-challenge performance, i.e., the decrement between the average of one hour of control and an hour at the time of maximum effect. Drugs with a different time course can reduce these periods and total test times to more convenient durations. Both tasks have demonstrated their capability to detect and measure intensity of dissociation whether latent or manifest, fluctuating spontaneously or waning with therapy in the ill or with prophylactic treatment in normals subjected to stress.

To facilitate the comparison of the objective, instrumental data so obtained with the total clinical picture, the latter is formalized by a weekly mental status rating filled out by the ward physician and another by the research nurse and by an abbreviated MMPI. These are converted by the computer into graphs of the items and of the item clusters. It is expected that the profiles derived from these can be analyzed for correspondence with those from the instrumental data. In a military or work situation a performance rating profile would be substituted for the clinical.

Special Military Pertinence

Our data using amphetamine to challenge accessibility of information suggest that the use of amphetamine to promote wakefulness in the military as well as in the student taking examinations is at the cost of impaired discriminating retrieval of information, and therefore inaccuracy and reduced reliability. These factors must be weighed and perhaps a new alerting agent or one combined with a corrective should be proposed and tested.

Additional complexity and pertinence to military operation could be achieved by combining the visual and auditory tests, approximating a military situation by making the visual task a three dimensional pursuit or tracking task requiring matching of visual tracking achieved by prompt voice commands giving appropriate instructions of suitable complexity - instructions which could be sent through filters that would not allow passage of impaired speech.

Calibration and Visual Perception Training Capability

The need for a ready calibration system in the visual perceptual conflict testing that would, preferably, utilize the same tracking procedure required the induction of a known degree of visual distortion that did not depend on binocular fusion, since the operation of the mental process required in the latter is not standardized simply. The procedure also proved useful in recognizing failure to attend and malingering, as well as for training in the few individuals who required more than a simple preliminary session for this purpose.

All of these objectives are now accomplished by optically, actually tilting a wall of the test room a given number of degrees and requiring a matching tilt of the guide bar by the subject. The required wall rotation is accomplished by tilting the viewing mirror of a periscopic mirror system slid into place behind the viewing aperture. Training is facilitated by rewarding a correct match. When desired, short "refresher" training segments can be interspersed with regular segments of the testing.

Projected Further Work

1. More controls with subjects of matching ages are needed.
2. Further validation is to be attempted by demonstration of concordance between objective, instrumental testing and the computerized clinical evaluations.
3. To make visual perceptual testing as feasible for field work as the auditory visual perceptual testing already is, it will be necessary to miniaturize the former.
4. Use of a challenging agent with a shorter time course would serve to both desirably shorten the test period and produce a sharper peak in the post-challenge portion of the curve.
5. Tooling-up is proceeding for the recording of human cerebral evoked potentials from scalp electrodes to support the animal data already obtained.

SUMMARY

1. A critical aspect of the problem of "Aerospace Stress and Human Reliability" has been identified as a fundamental factor in coping behavior in which specific performance

depends on adequate use of past experience, including special training to generate appropriate responses. These may be close copies of previous performances or modifications suitable to the relation of the new situation to the model generalized from the sum of related past experiences. The required mobilization of past experience starts with information retrieval.

2. A neurophysiological basis for impaired information retrieval follows from the findings: -

- A. Cerebral homeostasis is, in the first instance, dependent upon synaptic neuro-humoral equilibria. The electrical monitoring of synaptic transmission by evoked potentials was facilitated by an optical scanner of filmed oscilloscope traces that was developed and by a computer measuring program that was devised for these, taken either from the scanner or directly from the oscilloscope input terminals.
- B. Drug characterization of cerebral synapses reveals the generalization that they all react in qualitatively the same manner with individual differences that are only quantitative. These findings have been substantiated at the cortical, sub-cortical, brain stem and cerebellar levels. The predictive value of this generalization is confirmed by tests with thirty-six drugs. The differences in threshold are the clue to the disorganizing effects of attempts to influence neuro-humoral transmission, and conversely, the possibilities for correction when functional disorganization is already present.
- C. The finding of low thresholds of association areas to cerebral synaptic inhibitors provides a basis for the dissociation with impairment of information retrieval that occurs in hallucination, and which can be experimentally reproduced, at will, with hallucinogens and other dissociating drugs. The animal and human behavioral effects support this view.

3. On the basis of the above a practical test was devised to measure important deficits

in the human capacity for reliability. The test devised to meet Air Force needs met the following specifications:

- A. That, since information retrieval is the initial, basic step in performance it is an essential and probably most important factor to be measured in assessing the reliability of a trained person, who is not expected to have motor incoordination of a primary origin, i.e., other than due to uncertainty resulting from impaired decision making to which, among others, an inadequate proprioceptive information feed-back contributes.
- B. Objective, instrumental, simple tests are required that can be carried out by relatively non-skilled personnel in the field, and that are easy to analyze either locally, or centrally. In the latter case analysis could be facilitated by computerization.
- C. Identity and nature of testing should not be so obtrusive as to be disturbing to subjects and prevent acceptance as a routine procedure.
- D. Testing should be a valid predictor of "break-down point" under stress without actually "breaking down" or impairing normal performance immediately subsequent to or as an aftermath of the testing.
- E. Testing should be capable of detecting latent difficulties that may never have become overt to date, but possibly could be corrected without ever becoming overt.
- F. Testing should be capable of detecting undue rigidity in the manner in which subjects relate to environment with loss, therefore, of adequate flexibility to adapt to and solve infrequent or even unforeseen situations.

4. The tests developed utilized sub-clinical (i.e., producing no overt symptoms) amounts of challenging agents to which normal college students adapted and therefore showed no change, whereas patients and children with reduced reliability (behaviorally disturbed)

showed proportionate changes.

5. A computerized display of formalized behavioral assessment in the form of rating scales and the MMPI are being used to test concordance with the instrumental testing described to supply validation acceptable to the clinician and the qualifying officers.

6. Use by the military would allow: -

1. Screening for suitable personnel.

2. Periodic testing for:

A. Reliability status and possible need for "refresher" training.

B. Efficacy of training.

3. Pre- and post-combat reliability evaluation and qualifying for subsequent additional missions.

4. Field testing of drugs to improve reliability under stress.

7. Extension to the clinical field allows us to:

A. Propose a testable concept of hallucination based on information deficit and on information excess.

B. Recognize psychosis as a failure of integration or cerebral homeostasis.

C. Provide a screening test for latent mental illness.

D. Provide an objective, instrumental diagnostic procedure for mental illness, including the monitoring of its intensity and response to therapy.

E. Provide a human test for candidate therapeutic agents in the treatment of mental illness.

The clinical extensions of the testing described could aid in ushering in an era of more practical preventive psychiatry based on measurement of latent pathological function and its degree of regression under treatment.

(cont.)

PROPOSED FURTHER WORK

1. Military Applications Requiring Authorization

The full benefit of the investment in the project, "Aerospace Stress and Human Reliability", can be realized only by field trial as soon as possible. Our proximity to the Scott Air Force Base suggests that it would be ideal to make an early beginning at this location.

It would readily be possible to train teams at this and at other bases and direct supervision could be supplied when necessary most readily at the near by base and at other bases by planned visits. The data could be processed at the base or at our laboratories.

The trials would be designed for screening of recruits and of personnel for special missions. They would also be properly used for further qualifying personnel for special missions and to determine the effects of combat and the adequacy of appropriate training procedures.

2. Drug Abuse Detection

Drug abuse represents essentially an effort to recreate aspects of mental dissociation which may be found pleasurable or serve to attempt a solution to problems posed by the environment, by changing the perception of the environment to what the user may find or believes to be a more acceptable substitute.

Since the techniques we have developed can measure this self-induced dissociation, they offer the possibility of detecting by direct measurement of the mental status: -

1. When the user is under the influence of his drug abuse even though there are, at the time of testing, no overt manifestations. Since dissociation may, in fact, have persisting consequences because of resetting the nervous system, it may be possible to identify a drug abuser even when he is not on a "trip".
2. Potential long-lasting consequences in the form of disturbed cerebral integration.

The potential masking of the effects of the challenging drug because of tolerance developed from previous exposure can be minimized by using as the challenge a dissociating agent that generally is not available to drug "users". This is so because cross tolerance appears to be

minimal. In fact, this permits tentative, indirect identification on a functional basis of the actual drug of abuse, if the subject is using it constantly or if he had used it within a week, by a reduced effect due to tolerance. That is, tolerance will reduce the effect of the challenger, when it is the same as the drug of abuse, compared to the effect of the "non-available" test agent to which, therefore, there would be no tolerance.

Such a procedure might even be able to detect those small numbers of insightful "users", who are able to train themselves to dissociate at will without drugs, in the manner of the accomplished mystic, and consequently would be more sensitive to the test drug. Presumably they might then respond to a smaller dose of test agent by its cueing effect in activating the trained dissociating process. In the same way, it might pick up those users who are subject to the so-called LSD "flash-back" recurrence of symptoms; if the latter is, in fact, a recognition of a minor hallucinatory process that might otherwise have gone unnoticed by the drug inexperienced and accordingly "untrained" subject.

3. Detection of Other Brain Function Dissociations of High Military Pertinence

A longer range proposal is to extend the inquiry into other types of dissociation that are of potential high military significance. These would be studies on the failure of cerebral integration that manifests itself as a loss of adequate control over emotion and motivation. Animal experiments would precede the significantly appropriate possibility of such studies in psychiatrically disturbed or latently disturbed patients; to be followed by similar tests of military personnel. Such studies would also include the possibilities, after adequate analysis, of supplying appropriate strengthening training and adequate testing of the effectiveness of the same.

Does not the veteran soldier who has learned to keep cool turn out to be the more efficient and more deadly military weapon?

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